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Inside this issue: STIs and sexual health awareness month

Sexually transmitted infections (STIs) continue to increase in Canada and this trend is consistent with much of the western world. Each STI presents unique challenges. Chlamydia is typically asymptomatic and syphilis goes into dormant periods. The treatment of gonorrhea has been complicated by the growing antimicrobial resistance to many of the previous first line antibiotics. See how you can gain easy access to the Agency's STI Guidelines through a new mobile app.

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Upcoming conference

April 16-18, 2015. **Association of Medical Microbiology and Infectious Disease (AMMI) Canada.** Annual Conference, Charlottetown, Prince Edward Island.
http://ammi.ca/annual-conference/2015/

Useful links

Public Health Agency of Canada. **Canadian Guidelines on Sexually Transmitted Infections**
App Store for Apple (iOS) devices:
https://itunes.apple.com/ca/app/canadian-guidelines-on-sexually/id958263397?mt=8
Google play for Android devices:
https://play.google.com/store/apps/details?id=ca.gc.hcsc.sti

Government of Canada. **Sexual Health**
http://healthycanadians.gc.ca/healthy-living-vie-saine/sexual-sexuelle/index-eng.php?_ga=1.125934925.1575686084.1412886377

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Canada

Chlamydia and lymphogranuloma venereum in Canada: 2003-2012 Summary Report

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Abstract

Background: Chlamydia continues to be the most commonly reported sexually transmitted infection in Canada. Lymphogranuloma venereum (LGV), caused by certain serovars of *Chlamydia trachomatis*, is becoming established in some populations in a number of Western countries.

Objective: To identify trends in reported cases of chlamydia and LGV in Canada from January 1, 2003 to December 31, 2012.

Methods: Notifiable disease data on chlamydia were submitted to the Public Health Agency of Canada by provincial and territorial epidemiological units and summarized at the national level by age and sex. Confirmatory testing for suspected LGV cases and serovar subtyping were performed by the National Microbiology Laboratory (NML). Where possible, provincial/territorial health authorities use a standardized national case report form to collect enhanced epidemiological data on each case and to submit the data to the Agency.

Results: Rates of reported cases of chlamydia increased by 57.6%, from 189.6 to 298.7 per 100,000 between 2003 and 2012. The rate of reported cases of chlamydia among females (383.5 per 100,000) was almost twice as high as that among males (212.0 per 100,000), although the highest relative rate increase occurred among males. In both males and females, the rates of chlamydia were highest in those aged 20 to 24 years. From 2004 to 2012, 170 cases of LGV were reported to the Agency by provincial health authorities (including 104 confirmed and 66 probable cases). In 2012, case reports were received on 12 confirmed and probable cases, compared to 38 laboratory-positive cases confirmed by the NML.

Conclusion: In Canada, as in many countries, chlamydia rates have markedly increased over the last 10 years, in part due to improved diagnosis through nucleic acid amplification (NAAT) testing. Consistent with trends in Europe and other countries, LGV is emerging in Canada among men who have sex with men (MSM).

Introduction

Chlamydia

Chlamydia has been nationally notifiable since 1991. It is a genital infection caused by the bacterium *Chlamydia trachomatis* and is the most commonly reported sexually transmitted infection (STI) in Canada. Infections are often asymptomatic in both males and females. In the absence of screening, these infections remain undiagnosed and contribute to the spread of chlamydia in sexually active individuals (1). A common complication associated with untreated and recurring chlamydia in females is pelvic inflammatory disease, which can lead to chronic pelvic pain, ectopic pregnancy and infertility. In males, complications are rarer but include epididymo-orchitis and infertility. Untreated chlamydia in pregnant women can be transmitted to their newborns, causing neonatal conjunctivitis or pneumonia. As with other STIs, chlamydia increases infection with and transmission of the human immunodeficiency virus (HIV). It recruits target cells for HIV to the genital tract and increases the shedding of HIV-infected cells (2, 3).

Between 1991 and 1997, the rate of reported cases of chlamydia decreased steadily among both males and females, after which rates began to rise (4).

Lymphogranuloma venereum

Lymphogranuloma venereum (LGV) is an STI caused by *C. trachomatis* serovars L1, L2 and L3. Infections caused by these serovars preferentially invade lymph tissue and tend to be more invasive than those caused by non-LGV chlamydia. Signs and symptoms include painful, ulcerative proctitis, with inguinal and/or femoral lymphadenopathy or buboes, accompanied by fever, myalgia and arthralgia.

Untreated LGV infection can result in severe complications including destruction of rectal and genital tissue. Although uncommon, in some cases, meningoencephalitis, hepatitis and death can also occur.

LGV is endemic in parts of Africa, Asia, South America and the Caribbean region and was relatively uncommon in Canada until 2003 (5). At that time, outbreaks of LGV began occurring among men who have sex with men in urban centres in Canada (6). Outbreaks among MSM have also been reported in European countries and the United States (7, 8, 9, 10). Recent data suggest that the infection has become endemic in the MSM population in some of these countries (11). In response to the emergence of LGV in Europe, Canada initiated enhanced surveillance of this STI in 2005 which included retrospective data from 2004.

The objective of this report is to summarize the trends in chlamydia and LGV rates in Canada between 2003 and 2012. It is based on the Report on Sexually Transmitted Infections in Canada: 2012 prepared by the Centre for Communicable Diseases and Infection Control of the Public Health Agency of Canada (PHAC) (available online) (12) and a supplementary statement on LGV (13).

Methods

Data collection

Data on laboratory-confirmed chlamydia cases were reported to the Canadian Notifiable Disease Surveillance System (CNDSS) by provincial and territorial health authorities according to the Agency's Case Definitions for Communicable Diseases under National Surveillance (14) (see box below). Data are submitted in a variety of formats (e.g., line-listed electronic, paper-based case reports, or aggregate data) and are verified and loaded into the CNDSS database by Agency personnel.

Confirmatory testing for suspected LGV cases is performed by the National Microbiology Laboratory (NML) by nucleic acid amplification testing (NAAT) and data on these cases are then shared with the Centre for Communicable Disease and Infection Control (CCDIC). Diagnosis of probable cases is based on serological testing alone and is done at provincial laboratories. Where possible, provincial/territorial health authorities use a standardized national case report form to collect enhanced epidemiological data on confirmed and probable cases and submit the data directly to CCDIC. At the current time, it is not possible to link case report forms on confirmed cases submitted to CCDIC with their corresponding NML data.

Case definitions of chlamydia and lymphogranuloma venereum (LGV)

Chlamydia: (14)

Laboratory evidence of infection in genitourinary and extra-genital specimens:

- Detection of *Chlamydia trachomatis* by culture,

OR

- Detection of *C. trachomatis* nucleic acid,

OR

- Detection of *C. trachomatis* antigen.

Lymphogranuloma venereum (LGV): (13)

- Laboratory evidence of *C. trachomatis* L1, L2 or L3 by positive NAAT testing.

Data analysis

Chlamydia data extracted from the CNDSS were analyzed by CCDIC staff. Rates were calculated by age group and sex using population estimates obtained from the Statistics Canada Demography Division. Rate change calculations were made on unrounded figures for greater precision.

Counts of LGV cases reported by the NML and by provincial/territorial health authorities are included separately, as there is currently no method of linking these two data sources. Confirmed cases reported by the NML may duplicate confirmed cases also reported by the provinces, but this degree of overlap is difficult to quantify.

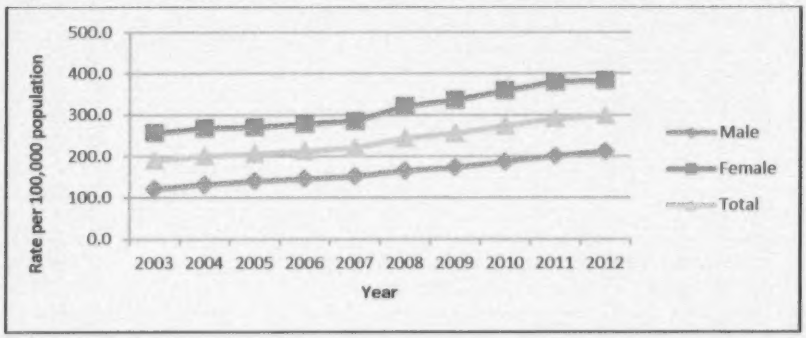
Surveillance is considered to be within the mandate of F/P/T programs and does not constitute human research; therefore, no research ethics board approval was sought.

Results

Chlamydia

In 2012, 103,716 cases of chlamydia were reported, corresponding to a rate of 298.7 per 100,000. The 2012 rate was a 57.6% increase from the rate of 189.6 per 100,000 in 2003. Among males, rates increased by 74.8%, from 121.3 to 212.0 per 100,000; among females, rates increased by 49.5%, from 256.5 to 383.5 per 100,000 **(Figure 1).**

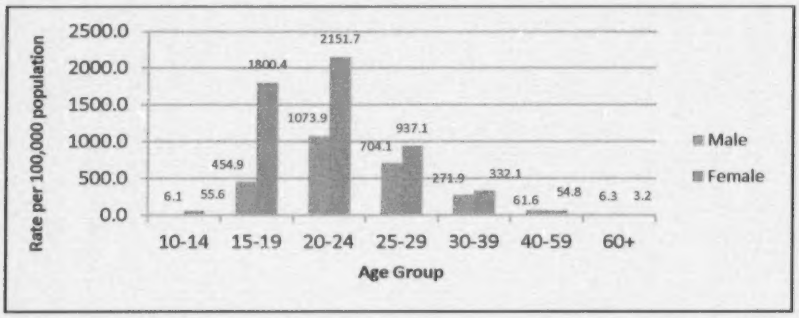
Figure 1: Overall and sex-specific rates of reported chlamydia cases, 2003 to 2012, Canada)



In 2012, rates were almost twice as high among females as compared to males and the majority (80.2%) of reported chlamydia infections occurred in persons under 30 years **(Figure 2).** In 2012, the highest rates were in the age 20 to 24 age group, though rates in females were twice as high as in males of this age (2151.7 per 100,000 vs. 1073.9 per 100,000, respectively). Among older age groups, the gap between sexes was less pronounced and even reversed; in 2012, the rates of reported cases were higher among men than women in those aged 40 and older **(Figure 2)**.

Between 2003 and 2012, rates of reported cases of chlamydia increased steadily among both males and females aged 10 and above. The highest relative rate increase occurred among those aged 10 to 14 (167.0%) while the highest relative rate increase in females occurred among those aged 60 and over (266.8%) (data not shown).

Figure 2: Rates of reported chlamydia cases by sex and age group, 2012, Canada



Lymphogranuloma venereum

As of December 2012, 170 cases were reported to the Agency by provincial health authorities (including 104 confirmed and 66 probable cases) **(Table 1)**. All confirmed cases were male and predominantly MSM. In 2012 alone, there were eight confirmed and four probable cases reported by the provinces and territories, however, there were 38 laboratory-confirmed cases reported by the NML.

Table 1: Reported confirmed and probable cases of lymphogranuloma venereum, 2004-2012, Canada

Year	Confirmed (NML)	Confirmed (case report form)	Probable (case report form)
2004	1	3	7
2005	37	36	21
2006	N/A	26	16
2007	N/A	1	7
2008	N/A	1	4
2009	N/A	9	0
2010	18	9	2
2011	34	11	5
2012	38	8	4
Total	**128**	**104**	**66**

Discussion

Increases in the rates of reported cases of chlamydia have been observed in Canada over the last decade. There are several factors that must be taken into account when considering these data.

The introduction of more sensitive nucleic acid amplification testing (NAAT) in the mid-1990s undoubtedly led to an increase in the number of chlamydia cases detected. NAAT allows urine specimens to be used rather than swabs, which are easier to collect and more acceptable to patients. As a result, the number of people, particularly males, who go for testing has likely increased as well. More effective screening and contact tracing may have a similar effect (15, 16). A recent estimation of chlamydia disease burden in Canada found that observed increases in chlamydia prevalence could be explained by effective case finding and expansion of screening programs (17).

Over time, the rate of reported cases of chlamydia has consistently been approximately twice as high in females as in males; however, this disparity is much more pronounced in younger age groups. Younger women are biologically more susceptible to chlamydial infection (18, 19). In addition, women are more likely to be screened for STIs (20, 21).

Trends in LGV infection are difficult to interpret due to gaps in available data, but there is evidence that it is becoming endemic among MSM in Canada. Early surveillance efforts were intensive, followed by a period of time (2007-2009) when few cases were reported. The more recent increase in cases beginning in 2010 and continuing into 2012 likely reflects improved case finding and reporting (22).

National guidelines for the prevention and management of chlamydial infections are available (2, 23) and treatment guidelines for LGV have recently been updated (13).

Acknowledgements

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Conflict of interest

None

Funding

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References

(1) Stamm WE. *Chlamydia trachomatis* infections of the adult. In: Holmes KK, Sparling PF, Mardh P, Lemon SM, Stamm WE, Piot P, et al., editors. Sexually transmitted diseases. 3rd ed. New York: McGraw-Hill; 1999. p. 407-422.

(2) Expert Working Group for the Canadian Guidelines on Sexually Transmitted Infections. Chlamydial Infections. In: Wong T, Latham-Carmanico C, editors. Canadian guidelines on sexually transmitted infections. 2010 ed. Ottawa: Public Health Agency of Canada; 2010.

(3) Fleming DT, Wasserheit JN. From epidemiological synergy to public health policy and practice: The contribution of other sexually transmitted diseases to sexual transmission of HIV infection. Sex Transm Infect. 1999 Feb;75(1):3-17.

(4) Public Health Agency of Canada. Report on sexually transmitted infections in Canada: 2011. Centre for Communicable Diseases and Infection Control, Infectious Disease Prevention and Control Branch, Public Health Agency of Canada; 2014. http://publications.gc.ca/site/eng/469949/publication.html.

(5) Expert Working Group for the Canadian Guidelines on Sexually Transmitted Infections. Lymphogranuloma venereum (LGV). In: Wong T, Latham-Carmanico C, editors. Canadian Guidelines on Sexually Transmitted Infections. 2010 ed. Ottawa: Public Health Agency of Canada; 2010.

(6) Kropp RY, Wong T, Canadian LGV Working Group. Emergence of lymphogranuloma venereum in Canada. CMAJ. 2005 Jun 21;172(13):1674-1676.

(7) Bremer V, Meyer T, Marcus U, Hamouda O. Lymphogranuloma venereum emerging in men who have sex with men in Germany. Euro Surveill. 2006 Sep;11(9):152-154.

(8) Koedijk FD, de Boer IM, de Vries HJ, Thiesbrummel HF, van der Sande MA. An ongoing outbreak of lymphogranuloma venereum in the Netherlands, 2006-2007. Euro Surveill. 2007 Apr 19;12(4):E070419.2.

(9) Jebbari H, Alexander S, Ward H, Evans B, Solomou M, Thornton A, et al. Update on lymphogranuloma venereum in the United Kingdom. Sex Transm Infect. 2007 Jul;83(4):324-326.

(10) HIV, STD and Hepatitis Prevention Branch, Public Health Services, Health and Human Services Agency, San Diego County. Lymphogranuloma venereum (LGV) update. 2005.

(11) Savage EJ, van de Laar MJ, Gallay A, van der Sande M, Hamouda O, Sasse A, et al. Lymphogranuloma venereum in Europe, 2003-2008. Euro Surveill. 2009 Dec 3;14(48):19428.

(12) Public Health Agency of Canada. Report on sexually transmitted infections in Canada: 2012. Centre for Communicable Diseases and Infection Control, Infectious Disease Prevention and Control Branch, Public Health Agency of Canada; 2015.

(13) Public Health Agency of Canada. A supplementary statement concerning the laboratory diagnosis of LGV. Canadian guidelines on sexually transmitted tnfections. http://www.phac-aspc.gc.ca/std-mts/sti-its/cgsti-ldcits/supp-lgv-eng.php

(14) Public Health Agency of Canada. Case definitions for communicable diseases under national surveillance Can Comm Dis Report. 2009; 35;S-2.

(15) McKay A, Barrett M. Rising reported rates of chlamydia among young women in Canada: What do they tell us about trends in the actual prevalence of the infection? Can J Hum Sex. 2008;17(1-2):61-69.

(16) Rekart ML, Brunham RC. Epidemiology of chlamydial infection: Are we losing ground? Sex Transm Infect. 2008 Apr;84(2):87-91.

(17) Tuite AR, Jayaraman GC, Allen VG, Fisman DN. Estimation of the burden of disease and costs of genital *Chlamydia trachomatis* infection in Canada. Sex Transm Dis. 2012 Apr;39(4):260-267.

(18) Lee V, Tobin JM, Foley E. Relationship of cervical ectopy to chlamydia infection in young women. J Fam Plann Reprod Health Care. 2006 Apr;32(2):104-106.

(19) Junior JE, Giraldo PC, Goncalves AK, do Amaral RL, Linhares IM. Uterine cervical ectopy during reproductive age: Cytological and microbiological findings. Diagn Cytopathol. 2014 May;42(5):401-404.

(20) Riera-Montes M, Velicko I. The chlamydia surveillance system in Sweden delivers relevant and accurate data: Results from the system evaluation, 1997-2008. Euro Surveill. 2011 Jul 7;16(27):19907.

(21) Machalek K, Hanley B, Kajiwara J, Pasquali P, Stannard C. Chlamydia screening practices among physicians and community nurses in Yukon, Canada. Int J Circumpolar Health. 2013;72(22447).

(22) Linedegger M, Salway Hottes T, Gilbert M, Lester R, Imperial M, Hoang L. Lymphogranuloma venereum in British Columbia: 2004 to 2011. Epidemiology and Surveillance, Clinical Prevention Services 2012.

(23) Public Health Agency of Canada. Canadian guidelines for sexual health education. Ottawa: Public Health Agency of Canada; 2008.

Gonorrhea in Canada: 2003-2012

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Abstract

Background: Gonorrhea is the second most commonly reported sexually transmitted infection in Canada. Between 1991 and 1997, Canada experienced a sharp decline in the rates of reported cases of gonorrhea, followed by a steady incline.

Objective: To identify trends in reported cases of gonorrhea in Canada from January 1, 2003 to December 31, 2012.

Methods: Notifiable disease reports were submitted to the Public Health Agency of Canada by provincial and territorial epidemiological units and data were summarized by age and sex.

Results: Between 2003 and 2012, the rate of reported cases of gonorrhea increased by 38.9%, from 26.0 to 36.2 per 100,000. Over this time frame, a greater relative rate increase was observed in females, though rates of gonorrhea increased in both sexes and across all age groups. In 2012, as in previous years, the rate of reported cases of gonorrhea was higher in males than females (41.4 vs. 31.0 per 100,000). Females between the ages of 15 and 24 years and males between the ages of 20 and 29 years accounted for the highest rates of gonorrhea in 2012.

Conclusion: In Canada, as in many countries, gonorrhea is on the rise, especially in young adults. This increase in rates of reported cases is in part due to improved diagnosis through nucleic acid amplification (NAAT) testing and may also be affected by growing gonococcal resistance to many available treatments.

Introduction

Gonorrhea has been nationally notifiable since 1924 and is the second most commonly reported sexually-transmitted infection (STI) in Canada. Gonorrhea is a genital bacterial infection caused by *Neisseria gonorrhoeae* and if left untreated, can lead to complications for both sexes. There can be severe consequences for females, including pelvic inflammatory disease, which often leads to chronic abdominal pain, infertility and ectopic pregnancy. In males, untreated infections can result in epididymitis and rare cases of infertility. An uncommon complication of gonorrhea is the spread of infection to the blood stream and joints (1). Like other STIs, gonorrhea increases the risk of HIV acquisition and transmission, possibly by increasing the concentration of HIV target cells in genital secretions and viral shedding (2).

Between 1991 and 1997, Canada experienced a sharp decline in the rates of reported cases of gonorrhea and rates were similar between males and females. After 1997, rates began to rise (3).

The objective of this report is to summarize the trends in gonorrhea rates in Canada between 2003 and 2012. It is based on the Report on Sexually Transmitted Infections in Canada: 2012 prepared by the Centre for Communicable Diseases and Infection Control of the Public Health Agency of Canada (PHAC) (available online) (4).

Methods

Data collection

Data on laboratory-confirmed gonorrhea cases were reported to the Canadian Notifiable Disease Surveillance System (CNDSS) by provincial and territorial health authorities according to the Agency's Case Definitions for Communicable Diseases under National Surveillance (5) (see box below). Data are submitted in a variety of formats (e.g., line-listed electronic, paper-based case reports, or aggregate data) and are verified and loaded into the CNDSS database by Agency personnel.

Case definitions of confirmed case of gonorrhea

Laboratory-evidence of infection in genitourinary or extra-genital specimens:

- Detection of *Neisseria gonorrhoeae* by culture,

OR

- Detection of *N. gonorrhoeae* nucleic acid.

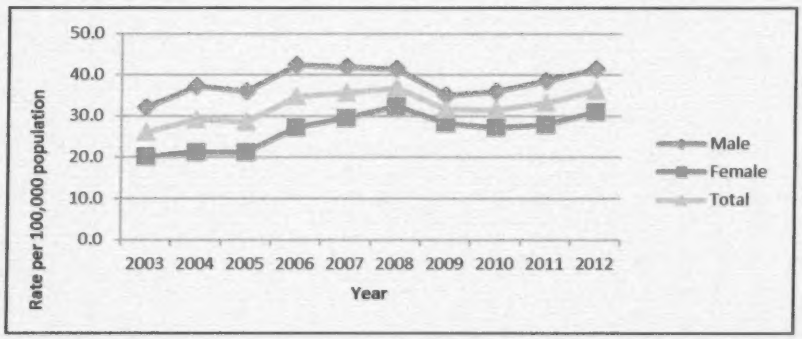
Data analysis

Gonorrhea data extracted from the CNDSS were analyzed by Centre for Communicable Diseases and Infection Control (CCDIC) staff. Rates were calculated by age group and sex using population estimates obtained from the Statistics Canada Demography Division. Rate change calculations were made on unrounded figures for greater precision. Surveillance is considered to be within the mandate of Federal/Provincial/Territorial (F/P/T) programs and does not constitute human research; therefore, no research ethics board approval was sought.

Results

In 2012, 12,561 cases of gonorrhea were reported through the CNDSS, corresponding to a rate of 36.2 per 100,000. The 2012 rate was a 38.9% increase from the rate of 26.0 per 100,000 in 2003. Over this ten-year time frame, rates increased among both males and females; males experienced a 29.1% relative rate increase while females experienced a 53.9% relative rate increase. Around 2006, rates of reported cases of gonorrhea began to show signs of stabilizing, with minor fluctuations from year to year. **(Figure 1)**.

Figure 1: Overall and sex-specific rates of gonorrhea, 2003 to 2012, Canada

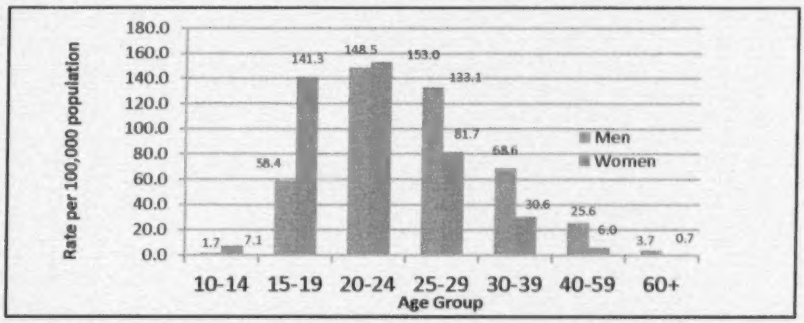


Rates of reported cases of gonorrhea in 2012 were higher among females than males in those less than 25 years of age; but were higher in males than females among those aged 25 years and over **(Figure 2)**. The highest rates of gonorrhea were observed among males and females aged 20 to 24.

Between 2003 and 2012, rates of reported cases of gonorrhea increased among both males and females aged 10 and above. The greatest relative rate increase observed among males was in those aged 10 to 14 years

(262.0%), from 0.5 to 1.7 per 100,000. Over this ten-year time frame, the highest relative increase observed among females was in those aged 60 and over (188.0%, from 0.2 to 0.7 per 100,000), though females in this age group exhibited the lowest rate of gonorrhea as compared to females in other age groups (data not shown).

Figure 2: Rates of reported gonorrhea by sex and age group, 2012, Canada



Between 2003 and 2012, most provinces and territories experienced a relative increase in the rate of the reported cases of gonorrhea (data not shown).

Discussion

Recent trends in the rates of reported cases of gonorrhea in Canada have shown overall increases, despite some year-to-year variation. The increases in rates since the late 1990s may be at least partly explained more sensitive testing methods and improved case finding (6).

Antimicrobial resistance may also play a significant role in the increase in reported rates of gonorrhea, as the proportion of isolates resistant to a number of antibiotics has increased over time, (7) which may lead to treatment failure and a longer duration of infectiousness in affected patients. Emerging antimicrobial resistance in gonorrhea has led to changes in treatment recommendations across Canada and elsewhere (8, 9, 10, 11).

In 2012, the overall rates of reported cases of gonorrhea were substantially lower in Canada at 36.2 per 100,000 compared to the United States (107.5 per 100,000) (12), Australia (58.9 per 100,000) (13) and England (48.1 per 100,000) (14). There was considerable variability in the differences observed across sexes; in Australia and England, gonorrhea rates were more than twice as high among males as compared to females, while the differences between sexes in Canada and the United States were less pronounced.

In conclusion, over a 10-year period, gonorrhea rates have increased almost 40% and these increases are particularly pronounced among young adults. While the reasons for these increases are likely multifactorial, it is possible that increasing gonococcal resistance to many available treatments has contributed to observed trends and should continue to be monitored.

Acknowledgements

The full report was prepared by the Centre for Communicable Diseases and Infection Control, Infectious Disease Prevention and Control Branch, Public Health Agency of Canada. Its publication would not have been possible without the collaboration of all provinces and territories, whose continuous contribution to national STI surveillance is greatly appreciated. The authors also acknowledge the contributions and expertise of the Sexually Transmitted and Blood-Borne Infections Surveillance Network.

Conflict of interest

None

Funding

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References

(1) Hook EW, Handsfield HH. Gonococcal infections in the adult. In: Holmes KK, Sparling PF, Mardh P, Lemon SM, Stamm WE, Piot P, et al., editors. Sexually transmitted diseases. 3rd ed. New York: Mc-Graw Hill; 1999. p. 451-466.

(2) Fleming DT, Wasserheit JN. From epidemiological synergy to public health policy and practice: The contribution of other sexually transmitted diseases to sexual transmission of HIV infection. Sex Transm Infect. 1999 Feb;75(1):3-17.

(3) Public Health Agency of Canada. Report on sexually transmitted infections in Canada: 2011. Centre for Communicable Diseases and Infection Control, Infectious Disease Prevention and Control Branch, Public Health Agency of Canada; 2014. 2011. http://publications.gc.ca/site/eng/469949/publication.html.

(4) Public Health Agency of Canada. Report on sexually transmitted infections in Canada: 2012. Centre for Communicable Diseases and Infection Control, Infectious Disease Prevention and Control Branch, Public Health Agency of Canada; 2015.

(5) Public Health Agency of Canada. Case definitions for communicable diseases under national surveillance Can Comm Dis Report. 2009; 35:S-2.

(6) Rekart ML, Brunham RC. Epidemiology of chlamydial infection: are we losing ground? Sex Transm Infect. 2008 Apr;84(2):87-91.

(7) Martin I, Sawatzky P, Liu G, Mulvey MR. Antimicrobial resistance to Neisseria gonorrhoeae in Canada: 2009-2013. CCDR. 2015 Feb;41(2).

(8) Plitt S, Boyington C, Sutherland K, Lovgren M, Tilley P, Read R, et al. Antimicrobial resistance in gonorrhea: The influence of epidemiologic and laboratory surveillance data on treatment guidelines: Alberta, Canada 2001-2007. Sex Transm Dis. 2009 Oct;36(10):665-669.

(9) Public Health Agency of Canada. Important notice: Public health information update on the treatment for gonococcal infection. 2011. http://www.phac-aspc.gc.ca/std-mts/sti-its/alert/2011/alert-gono-eng.php.

(10) Ontario Agency for Health Protection and Promotion (Public Health Ontario). Guidelines for testing and treatment of gonorrhea in Ontario. 2013.

(11) Centers for Disease Control and Prevention. Update to CDC's sexually transmitted diseases treatment guidelines, 2010: Oral cephalosporins no longer a recommended treatment for gonococcal infections. Morb Mortal Wkly Rep. 2012;61(31):590-594.

(12) Centers for Disease Control and Prevention. Sexually transmitted disease surveillance 2012. Atlanta: U.S. Department of Health and Human Services; 2013. http://www.cdc.gov/std/stats12/.

(13) The Kirby Institute. HIV, viral hepatitis and sexually transmissible infections. In Australia annual surveillance report 2013. The Kirby Institute, The University of New South Wales, Sydney NSW 2052. https://kirby.unsw.edu.au/surveillance/2013-annual-surveillance-report-hiv-viral-hepatitis-stis.

(14) Public Health England. Table 1: Number & rates of new STI diagnoses in England, 2003 – 2012. https://www.gov.uk/government/statistics.

Infectious syphilis in Canada: 2003-2012

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Abstract

Background: In the 1990s, rates of reported cases of infectious syphilis were relatively low and were similar among males and females. In 2001, rates began to increase, particularly among males.

Objective: To identify trends in reported cases of infectious syphilis in Canada from January 1, 2003 to December 31, 2012.

Methods: Notifiable disease reports were submitted to the Public Health Agency of Canada by provincial and territorial epidemiological units and data were summarized by age and sex.

Results: Rates of reported cases of infectious syphilis increased by 101.0% between 2003 and 2012, from 2.9 to 5.8 per 100,000. Over this time frame, rates increased among males by 128.3% and decreased among females by 40.9%. In males, rates of infectious syphilis were highest among those aged 25 to 29; in females, rates were highest among those aged 20 to 24.

Conclusion: In Canada, as in many countries, rates of reported infectious syphilis cases in males have markedly increased over the last 10 years.

Introduction

Syphilis has been nationally notifiable since 1924. It is caused by the bacterium *Treponema pallidum* and if left untreated, will progress through primary, secondary, latent and tertiary stages. Tertiary syphilis damages the central nervous system, cardiovascular system, eyes, skin and other internal organs (1). Individuals with early (symptomatic) syphilis infections are also at increased risk of contracting HIV and those co-infected with both pathogens are more likely to transmit HIV to their sexual partners (2). In co-infected individuals, there is a greater chance of rapid progression to serious consequential conditions, such as neurosyphilis, often while those individuals are still infectious (3, 4, 5). While all stages of syphilis are nationally notifiable, only primary, secondary and early latent syphilis (less than one year after the point of infection) are considered infectious and therefore are of major public health significance. As a result, only these stages are included in national reports.

From 1993 to 2001, rates of reported cases of infectious syphilis were very similar between males and females, with both sexes experiencing low rates (less than 1.0 per 100,000) over this time frame. In 2001, infectious syphilis rates began to climb sharply, particularly among males (6).

The objective of this report is to summarize the trends in infectious syphilis rates in Canada between 2003 and 2012. It is based on the Report on Sexually Transmitted Infections in Canada: 2012 prepared by the Centre for Communicable Diseases and Infection Control of the Public Health Agency of Canada (PHAC) (available online) (7).

Methods

Data collection

Data on laboratory-confirmed gonorrhea cases were reported to the Canadian Notifiable Disease Surveillance System (CNDSS) by provincial and territorial health authorities according to the Agency's Case Definitions for Communicable Diseases under National Surveillance (8) (see box below). Data are submitted in a variety of formats (e.g., line-listed electronic, paper-based case reports, or aggregate data) and are verified and loaded into the CNDSS database by Agency personnel.

Case definitions of infectious syphilis[1]

Primary Syphilis - Laboratory confirmation of infection:

Identification of *T. pallidum* by dark-field microscopy, fluorescent antibody, nucleic acid testing or equivalent examination of material from a chancre or a regional lymph node,

OR

Presence of one or more typical lesions (chancres) and reactive treponemal serology, regardless of non-treponemal test reactivity, in individuals with no previous history of syphilis,

OR

Presence of one or more typical lesions (chancres) and a fourfold or greater increase in the titre over the last known non-treponemal test in individuals with a past history of syphilis treatment.

Secondary Syphilis - Laboratory evidence of infection:

Identification of *T. pallidum* by dark-field microscopy, fluorescent antibody, nucleic acid testing or equivalent examination of mucocutaneous lesions, condylomata lata and reactive serology (non-treponemal and treponemal),

OR

Presence of typical signs or symptoms of secondary syphilis (e.g., mucocutaneous lesions, alopecia, loss of eyelashes and lateral third of eyebrows, iritis, generalized lymphadenopathy, fever, malaise or splenomegaly)

AND

Either a reactive serology (non-treponemal and treponemal OR a fourfold or greater increase in titre over the previous known non-treponemal test.

Early Latent Syphilis (< 1 year after infection) - Laboratory confirmation of infection:

An asymptomatic patient with reactive serology (treponemal and/or non-treponemal) who, within the previous 12 months, had one of the following: non-reactive serolog, symptoms suggestive of primary or secondary syphilis, exposure to a sexual partner with primary, secondary or early latent syphilis.

[1] For the purpose of this summary, congenital syphilis and (non-infectious) late latent syphilis were not included.

Data analysis

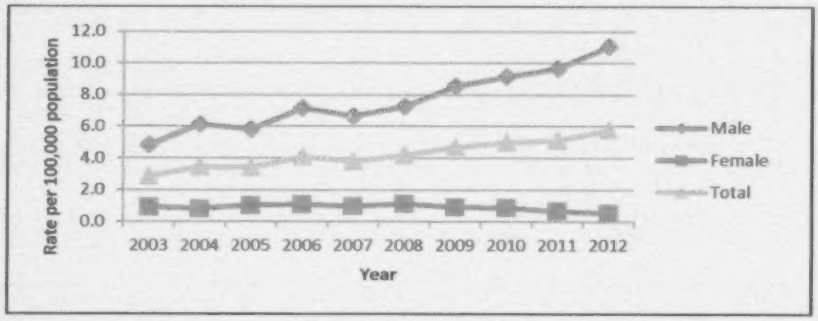
Infectious syphilis data extracted from the CNDSS were analyzed by Centre for Communicable Diseases and Infection Control (CCDIC) staff. Rates were calculated by age group and sex using population estimates obtained from the Statistics Canada Demography Division. Rate change calculations were made on unrounded figures for greater precision.

Surveillance is considered to be within the mandate of federal/provincial/territorial (F/P/T) programs and does not constitute human research; therefore, no research ethics board approval was sought.

Results

In 2012, 2003 cases of infectious syphilis were reported, corresponding to a rate of 5.8 per 100,000 and a 101.0% increase from the 2003 rate of 2.9 per 100,000. The majority of cases (94.9%) reported in 2012 were among men. Between 2003 and 2012, rates among males increased by 128.3% from 4.8 to 11.0 per 100,000; conversely, rates among females decreased by 40.9% from 0.9 to 0.5 per 100,000 **(Figure 1)**.

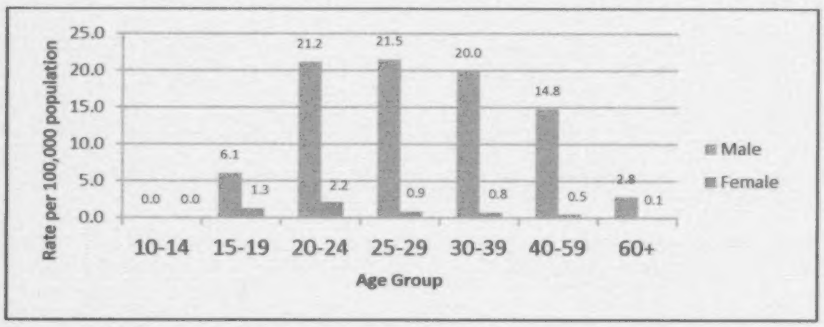
Figure 1: Overall and sex-specific rates of reported infectious syphilis, 2003 to 2012, Canada



As in previous years, in 2012, the majority (65.6%) of all reported cases of infectious syphilis were among men aged 30 years and older. The highest rates were among men aged 25 to 29 years, followed by men aged 20 to 24 years (21.5 and 21.2 per 100,000, respectively) **(Figure 2)**. Among women, rates of reported cases of infectious syphilis were substantially lower; the highest rates among women were observed among those aged 20 to 24 years, followed by those aged 15 to 19 years (2.2 and 1.3 per 100,000, respectively).

Between 2003 and 2012, relative rate increases were observed in males of all age groups, with the exception of those in the 10 to 14 age group (where zero cases were reported). Over the same period, rates decreased among females of all ages, with the exception of those aged 10 to 14 (where zero cases were reported) and those in the 15 to 19 age group where rates increased from 1.2 to 1.3 per 100,000 (data not shown).

Figure 2: Rates of reported infectious syphilis by sex and age group, 2012, Canada



Between 2003 and 2012, outbreaks of infectious syphilis were reported across most jurisdictions in Canada.

Discussion

After a near-zero incidence of infectious syphilis, the number of reported cases began to rise in 2001 and continues to do so, especially among males. There is a significant difference in rates between males and females. Rates have more than doubled in males in the last 10 years, whereas they have decreased by a little over 40% in females. This resurgence appears to be primarily due to transmission among men who have sex with men (MSM). Increasing sexually transmitted infection (STI) rates among MSM have also been observed in the United States

and Europe. The causes for these increases are complex and include demographic shifts as well as changing sexual attitudes and social contexts related to risky sexual practices (9).

There are several factors that must be taken into account when considering these data. For example, the number of cases of infectious syphilis in Canada is low relative to other STIs. As a result, population rates are variable and unstable and therefore changes over time should be interpreted with caution. That being said, the number of reported cases likely underestimates the true burden of infection; many people who are infected with syphilis do not have symptoms and therefore may not be tested by a health care practitioner.

Internationally, overall rates of infectious syphilis were lowest in the United States (5.0 per 100,000) (10), although this estimate does not include early latent cases. Among countries that included early latent syphilis cases, Australia had the highest rate (6.7 per 100,000) (11) and in England, the rate was 5.6 per 100,000 (12) compared to Canada's rate of 5.8 per 100,000. Variations in annual rates of infectious syphilis across countries should be interpreted with caution as a result of differing reporting practices.

In conclusion, over a 10-year period, Canada has witnessed a 40% decrease in syphilis rates in women and a 128% increase in syphilis rates in men, which is consistent with trends seen in other Western countries.

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Conflict of interest

None

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References

(1) Expert Working Group for the Canadian Guidelines on Sexually Transmitted Infections. Syphilis. In: Wong T, Latham-Carmanico C, editors. Canadian guidelines on sexually transmitted infections. 2010 ed. Ottawa: Public Health Agency of Canada; 2010.

(2) Fleming DT, Wasserheit JN. From epidemiological synergy to public health policy and practice: The contribution of other sexually transmitted diseases to sexual transmission of HIV infection. Sex Transm Infect. 1999 Feb;75(1):3-17.

(3) Buchacz K, Patel P, Taylor M, Kerndt PR, Byers RH, Holmberg SD, et al. Syphilis increases HIV viral load and decreases CD4 cell counts in HIV-infected patients with new syphilis infections. AIDS. 2004 Oct 21;18(15):2075-2079.

(4) Pialoux G, Vimont S, Moulignier A, Buteux M, Abraham B, Bonnard P. Effect of HIV infection on the course of syphilis. AIDS Rev. 2008 Apr-Jun;10(2):85-92.

(5) Narula T, Kamboj S, Martinez J, Engel LS. Co-infection: HIV and the great mimic syphilis. HIV Clin. 2010 Spring;22(2):7-10.

(6) Public Health Agency of Canada. Report on sexually transmitted infections in Canada: 2011. Centre for Communicable Diseases and Infection Control, Infectious Disease Prevention and Control Branch, Public Health Agency of Canada; 2015.

(7) Public Health Agency of Canada. Report on sexually transmitted infections in Canada: 2012. Centre for Communicable Diseases and Infection Control, Infectious Disease Prevention and Control Branch, Public Health Agency of Canada; 2015.

(8) Public Health Agency of Canada. Case definitions for communicable diseases under national surveillance. Can Comm Dis Report. 2009: 35; S-2.

(9) Fenton KA, Imrie J. Increasing rates of sexually transmitted diseases in homosexual men in Western Europe and the United States: Why? Infect Dis Clin North Am. 2005 Jun;19(2):311-331.

(10) Centers for Disease Control and Prevention. Sexually transmitted disease surveillance 2012. Atlanta: U.S. Department of Health and Human Services; 2013. http://www.cdc.gov/std/stats12/.

(11) The Kirby Institute. HIV, viral hepatitis and sexually transmissible infections. In Australia annual surveillance report 2013. The Kirby Institute, The University of New South Wales, Sydney NSW 2052. https://kirby.unsw.edu.au/surveillance/2013-annual-surveillance-report-hiv-viral-hepatitis-stis.

(12) Public Health England. Table 1: Number & rates of new STI diagnoses in England, 2003 – 2012. https://www.gov.uk/government/statistics.

Antimicrobial resistance to *Neisseria gonorrhoeae* in Canada: 2009-2013

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Abstract

Background: Gonorrhea is on the rise in Canada. Treatment has been complicated by the fact that *Neisseria gonorrhoeae* has acquired resistance to many antibiotics, including penicillin, tetracycline, erythromycin and ciprofloxacin. The emergence of isolates with decreased susceptibilities to the third generation cephalosporins and reports of treatment failures in Canada and around the world are cause for concern.

Objective: To assess the resistance levels of common antibiotics to *N. gonorrhoeae* and to observe trends in resistance and/or decreased susceptibility to ciprofloxacin, third generation cephalosporins and azithromycin.

Methods: Laboratory surveillance data for *N. gonorrhoeae* isolates submitted by provincial microbiology laboratories to the National Microbiology Laboratory (NML) from 2009-2013 were compared.

Results: Since 2009, there has been an overall rise in antibiotic-resistant *N. gonorrhoeae*. In 2013, 24.3% of the isolates were resistant to erythromycin, 18.9% were resistant to penicillin, 33.0% were resistant to tetracycline, and 29.3% were resistant to ciprofloxacin. The percentage of isolates with decreased susceptibility to ceftriaxone (≥0.125 mg/L) and/or cefixime (≥0.25 mg/L) was 3.9% in 2013. This number represents a decrease from 5.9% in 2012 and 7.6% in 2011. The proportion of azithromycin resistant (MIC ≥2 mg/L) *N. gonorrhoeae* isolates increased from 0.4% in 2009 to 1.2% in 2013.

Conclusion: Resistance to erythromycin, penicillin, tetracycline and ciprofloxacin is common. Decreased susceptibility to ceftriaxone and/or cefixime is now almost 4% and azithromycin resistance is emerging but remains low at 1.2%. These results have informed the gonococcal infection treatment recommendations in the Canadian Guidelines on Sexually Transmitted Infections.

Introduction

N. gonorrhoeae, the causative agent of gonorrhea, is the second most commonly reported bacterial sexually transmitted infection in Canada and rates of reported cases have more than doubled between 1997 and 2012 (1).

The treatment and control of gonorrhea is complicated by the ability of *N. gonorrhoeae* to evolve and develop resistance to many of the antibiotics used to treat it (2, 3). The emergence of isolates with decreased susceptibilities to the cephalosporins (4, 5, 6, 7) and reports of treatment failures in Canada (8) and around the world raises the possibility of gonorrhea infections becoming untreatable in the future. The emergence of high-level azithromycin resistant (≥256 mg/L) *N. gonorrhoeae* has been reported internationally (9) and isolates with this high level azithromycin resistance have now been identified in Canada.

The number of cultures available for antimicrobial susceptibility testing is on the decline due to the shift from the use of culture to Nucleic Acid Amplification Test (NAAT) for the diagnosis of gonorrhea. This is of concern as *N. gonorrhoeae* cultures are required for antimicrobial susceptibility testing and some jurisdictions in Canada no longer maintain the capacity to culture this organism. In fact, over 70% of gonococcal infections in Canada are now diagnosed using NAAT and therefore antimicrobial susceptibility data in these jurisdictions are not available. The National Microbiology Laboratory (NML), in collaboration with the provincial laboratories, has been monitoring the antimicrobial susceptibilities of *N. gonorrhoeae* since 1985.

The objective of this report is to summarize the trends in antimicrobial resistance to gonorrhea infections in Canada between 2009 and 2013. It is based on the National Surveillance of Antimicrobial Susceptibilities of *Neisseria gonorrhoeae* Annual Summary 2013 prepared by the NML, Public Health Agency of Canada (PHAC) (10).

Methods

Data collection

Provincial public health laboratories submitted a total of 5,518 viable *N. gonorrhoeae* isolates to the NML for antimicrobial susceptibility testing as part of the passive National *Neisseria gonorrhoeae* Surveillance Program between 2009 and 2013 (2009, N=913; 2010, N=1,233; 2011, N=1,158; 2012, N=1,031; 2013, N=1,183). *N. gonorrhoeae* isolates are submitted to the NML when the provincial laboratories identify resistance to at least one antibiotic or if the provincial laboratories do not perform any antimicrobial susceptibility testing. Submission of isolates is voluntary and is not standardized across the country. The overall interpretation of the results is difficult due to the limitations related to the isolates available for testing. Therefore, the total number of isolates cultured in all provinces was used as the denominator to calculate resistance proportion (2009, N=3,106; 2010, N=2,970; 2011, N=3,360; 2012, N=3,036; 2013, N=3,195).

MICs were determined by agar dilution (11) and resistance was defined according to the Clinical and Laboratory Standards Institute (11) except for erythromycin (12) and azithromycin (13). Decreased susceptibility breakpoints for ceftriaxone and cefixime were based on WHO definitions (14). Common abbreviations for the different types of resistance have been developed (**Table 1**).

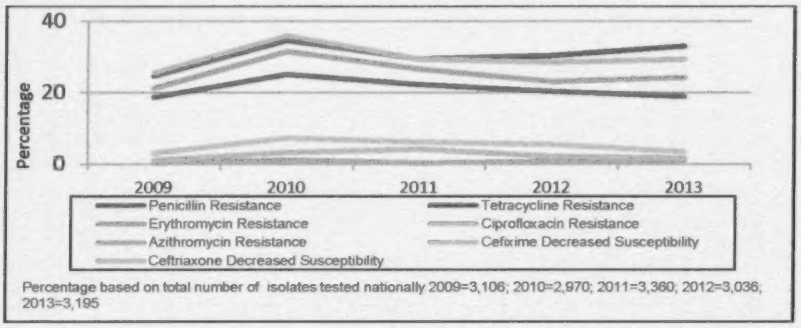
Table 1: Abbreviations and definitions for the different types of *Neisseria gonorrhoeae* antimicrobial resistance

Abbreviation	Term in full	Definition
PPNG	Penicillinase-Producing *N. gonorrhoeae*	Pen MIC ≥ 2.0 mg/L, β-lactamase positive, β-lactamase plasmid (3.05, 3.2 or 4.5 Mdal plasmid)
TRNG	Tetracycline Resistant *N. gonorrhoeae* (plasmid-mediated)	Tet MIC ≥ 16.0 mg/L, 25.2 Mdal plasmid, TetM PCR positive
CMRNG	Chromosomal Mediated Resistant *N. gonorrhoeae*	Pen MIC ≥ 2.0 mg/L, Tet MIC ≥ 2.0 mg/L but ≤ 8.0 mg/L and Ery MIC ≥ 2.0 mg/L
Probable CMRNG	Probable Chromosomal Mediated Resistant *N. gonorrhoeae*	One of the MIC values of Pen, Tet, Ery = 1 mg/L, the other two ≥ 2.0 mg/L
TetR	Tetracycline Resistant *N. gonorrhoeae* (chromosomal mediated)	Tet MIC ≥ 2.0 mg/L but ≤ 8.0 mg/L
CipR	Ciprofloxacin Resistant *N. gonorrhoeae*	Cip MIC ≥ 1.0 mg/L
AzR	Azithromycin Resistant *N. gonorrhoeae*	Az MIC ≥ 2.0 mg/L
SpecR	Spectinomycin Resistant *N. gonorrhoeae*	Spec R ≥ 128 mg/L
CxDS	*N. gonorrhoeae* with decreased susceptibility to Ceftriaxone	Cx MIC ≥ 0.125 mg/L
CeDS	*N. gonorrhoeae* with decreased susceptibility to Cefixime	Ce MIC ≥ 0.25 mg/L

Results

Figure 1 shows the trends of antimicrobial susceptibilities of *N. gonorrhoeae* tested in Canada from 2009 to 2013.

Figure 1: Trends of antimicrobial susceptibilities of *Neisseria gonorrhoeae* tested in Canada from 2009 to 2013



Of the 3,195 *N. gonorrhoeae* isolates cultured in public health laboratories across Canada in 2013, 1,183 presumptively resistant isolates were submitted to the NML. Of these, 1,153 were confirmed to be resistant to at least one antibiotic and 30 were susceptible which translates to 36.1% of all *N. gonorrhoeae* cases diagnosed by culture as resistant *N. gonorrhoeae*.

Gender and age data was available for 99.5% of the 2013 isolates tested at the NML. Of these, 83.1% were males ranging from 1 month to 74 years of age. A total of 16.9% of isolates were from females aged 2 to 71 years.

Third generation cephalosporins

In 2013, according to WHO definitions, 1.8% of isolates were identified as having decreased susceptibility to cefixime and 3.5% were identified as having decreased susceptibility to ceftriaxone. These rates are higher than they were in 2009 (1.2% decreased susceptibility to cefixime and 3.1% decreased susceptibility to ceftriaxone), but lower than in 2011 (4.2% decreased susceptibility to cefixime and 6.2% decreased susceptibility to ceftriaxone). In 2013, 3.9% of isolates were identified with decreased susceptibility to ceftriaxone and/or cefixime decreasing from 5.9% in 2012 and 7.6% in 2011.

Azithromycin

Azithromycin resistant *N. gonorrhoeae* increased from 0.4% in 2009 to 1.2% in 2013. Between 2009 and 2012, five isolates with high-level azithromycin resistance (MIC ≥256 mg/L) were identified in Canada. The modal MIC for azithromycin has remained at 0.5 mg/L each year between 2009 and 2012. In 2013, the modal decreased to 0.25 mg/L.

In 2012, seven isolates with combined decreased susceptibility to cephalosporins and resistance to azithromycin were identified (0.2%). In 2013, eight (0.3%) of these isolates were identified. These are the first isolates to emerge in Canada with both decreased susceptibility to cephalosporins and resistance to azithromycin thus threatening the success of currently recommended dual therapy treatment options.

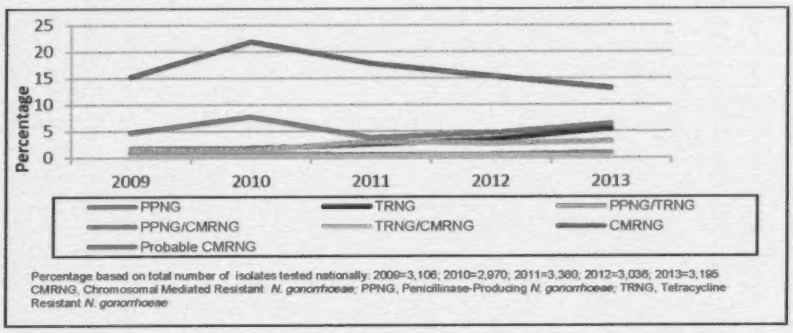
Other antibiotics

The percentage of ciprofloxacin resistant isolates increased from 25.5% in 2009 to 29.3% in 2013. Ciprofloxacin resistance increased from 1.3% in 2000 to a high of 36.0% in 2010. The modal MIC of ciprofloxacin has shifted dramatically from 0.004 mg/L in 2004 to 16.0 mg/L in 2013 (data not shown).

In 2009, 21.3% of isolates were found to be erythromycin resistant. This percentage increased to 31.5% by 2010 and then decreased to 24.3% by 2013. Penicillin resistance increased from 18.7% in 2009, to 25.1% in 2010 and then decreased to 18.9% in 2013. Tetracycline resistance increased from 24.7% in 2009 to 34.6% in 2010 and then decreased to 33.0% in 2013. Of the 5,518 viable isolates tested at NML between 2009 and 2013, none showed resistance to spectinomycin.

In 2013, 13.5% of isolates were classified as Chromosomal mediated resistant *N. gonorrhoeae* (CMRNG), a slight decrease from the 15.3% identified in 2009. Penicillinase-producing *N. gonorrhoeae* (PPNG) accounted for 4.3% in 2013, increasing slightly from 2.5% in 2009. Plasmid-mediated tetracycline resistant *N. gonorrhoeae* (TRNG) increased from 3.2% in 2009 to 8.8% of isolates in 2013 (**Figure 2**).

Figure 2: Trends in chromosomal and plasmid-mediated antimicrobial resistance in *Neisseria gonorrhoeae* in Canada from 2009 to 2013



Percentage based on total number of isolates tested nationally: 2009=3,106; 2010=2,970; 2011=3,380; 2012=3,036; 2013=3,195
CMRNG, Chromosomal Mediated Resistant *N. gonorrhoeae*; PPNG, Penicillinase-Producing *N. gonorrhoeae*; TRNG, Tetracycline Resistant *N. gonorrhoeae*

Discussion

The evolution of antimicrobial resistance in gonorrhea is complex and the emergence and spread of resistant isolates is a recognized global public health threat. Surveillance and monitoring of the antimicrobial susceptibilities of *N. gonorrhoeae* will continue to inform efforts to mitigate the impact of antimicrobial resistance in gonorrhea and guide therapeutic recommendations.

Reports of cefixime treatment failures and the observed MIC creep between 2001 and 2010 for both cefixime (from 0.016 mg/L to 0.125 mg/L) and ceftriaxone (from 0.016 mg/L to 0.063 mg/L) led to gonorrhea treatment changes. In 2011, the Canadian STI Guidelines issued updated recommendations for the use of combination gonorrhea therapy with 250 mg ceftriaxone intramuscularly and azithromycin 1 g orally as the first-line regimen in men-who-have-sex-with men (MSM) and in pharyngeal infections (15).

Since the 2011 changes to gonorrhea treatment recommendations in Canada there has been a decrease in the proportion of isolates with elevated MICs to the cephalosporins. In 2011, 7.6% of isolates exhibited decreased susceptibility to ceftriaxone and/or cefixime according to the WHO definition. This decreased to 5.9% in 2012 and further declined to 3.9% of isolates tested in 2013.

Fortunately, dropping rates of reduced cefixime susceptibility are also being seen elsewhere. For example, the US reported declines to decreased cefixime susceptibility from 3.9% in 2010 to 2.9% in the first half of 2012 (16). The UK reported the prevalence of isolates with decreased cefixime susceptibility dropped from 17.1% in 2010 to 10.8% in 2011 (17).

Enhancing surveillance to include linked epidemiological and laboratory data will assist with the limitations in the current passive surveillance system regarding data representativeness and interpretation. These improvements to the gonococcal surveillance program are expected with the Enhanced Surveillance of Antimicrobial Resistant Gonorrhea (ESAG) program beginning in 2014.

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Conflict of interest

None

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References

(1) Public Health Agency of Canada. Notifiable Diseases On-Line. 2014. http://dsol-smed.phac-aspc.gc.ca/dsol-smed/ndis/charts.php?c=pl.

(2) Barry PM, Klausner JD. The use of cephalosporins for gonorrhoea: The impending problem of resistance. Expert Opin Pharmacother. 2009; 10:555–577.

(3) Tapsall J. Antibiotic resistance in *Neisseria gonorrhoeae* is diminishing available treatment options for gonorrhoea: Some possible remedies. Expert Rev Anti Infect Ther. 2006; 4:619-628.

(4) Golparian D, Hellmark B, Fredlund H, Unemo M. Emergence, spread and characteristics of *Neisseria gonorrhoeae* isolates with in vitro decreased susceptibility and resistance to extended-spectrum cephalosporins in Sweden. Sex Transm Infect. 2010; 86:454-460.

(5) Ison CA, Hussey J, Sankar KN, Evans J, Alexander S. Gonorrhoea treatment failures to cefixime and azithromycin in England, 2010. Euro Surveill. 2011; 16(14):pii=19833.

(6) Pandori M, Barry PM, Wu A, Ren A, Whittington WLH, Liska S, Klausner JD. Mosaic penicillin-binding protein 2 in *Neisseria gonorrhoeae* isolates collected in 2008 in San Francisco, California. Antimicrob Agents Chemother. 2009; 53:4032-4034.

(7) World Health Organization (WHO). Emergence of multi-drug resistant *Neisseria gonorrhoeae*: Threat of global rise in untreatable sexually transmitted infections. 2011. http://whqlibdoc.who.int/hq/2011/WHO_RHR_11.14_eng.pdf.

(8) Allen VG, Mitterni L, Seah C, Rebbapragada A, Martin IE, Lee C, Siebert H, Towns L, Melano RG, Lowe DE. *Neisseria gonorrhoeae* treatment failure and susceptibility to cefixime in Toronto, Canada. JAMA. 2013; 309:163-170.

(9) Chisholm SA, Neal TJ, Alawattegama AB, Birley HDL, Howe RA, Ison CA. Emergence of high-level azithromycin resistance in *Neisseria gonorrhoeae* in England and Wales. J Antimicrob Chemother. 2009; 64:353-358.

(10) Public Health Agency of Canada. National Microbiology Laboratory. 2014. National surveillance of antimicrobial susceptibilities of *Neisseria gonorrhoeae* annual summary 2013.

(11) Clinical and Laboratory Standards Institute. Performance standards for antimicrobial susceptibility testing: Twenty-third informational supplement M100-S24 Vol. 34. Wayne, PA: Clinical and Laboratory Standards Institute; 2014.

(12) Ehret JM, Nims LJ, Judson FN. A clinical isolate of *Neisseria gonorrhoeae* with in vitro resistance to erythromycin and decreased susceptibility to azithromycin. Sex Transm Dis. 1996; 23:270-272.

(13) Centers for Disease Control and Prevention. Sexually transmitted disease surveillance 2007 Supplement, gonococcal isolate surveillance project (GISP) Annual report 2007. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, March 2009. http//www.cdc.gov/std/GISP2007/.

(14) World Health Organization (WHO). Global action plan to control the spread and impact of antimicrobial resistance in *Neisseria gonorrhoeae*. 2012. http://www.who.int/reproductivehealth/publications/rtis/9789241503501/en/.

(15) Public Health Agency of Canada, 2011. Important notice: Public health information update on the treatment of Gonococcal Infection. http://www.phac-aspc.gc.ca/std-mts/sti-its/alert/2011/alert-gono-eng.php.

(16) Kirkcaldy RD, Kidd S, Weinstock HS, Papp JR, Bolan GA. Trends in antimicrobial resistance in *Neisseria gonorrhoeae* in the USA: the Gonococcal Isolate Surveillance Project (GISP), January 2006–June 2012. Sex Transm Infect. 2013 Dec; 89 Suppl 4:iv5-10.

(17) Ison CA, Town K, Obi C, Chisholm S, Hughes G, Livermore DM, Lowndes CM, GRASP Collaborative Group. Decreased susceptibility to cephalosporins among gonococci: Data from the Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP) in England and Wales, 2007-2011. Lancet Infect Dis. 2013; 13:762-8.